



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,082	08/07/2001	Lawrence J. Marnett	N-7362 RSM	1831

32885 7590 12/01/2004
STITES & HARBISON PLLC
424 CHURCH STREET
SUITE 1800
NASHVILLE, TN 37219-2376

EXAMINER

PAK, YONG D

ART UNIT PAPER NUMBER

1652

DATE MAILED: 12/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/924,082

Applicant(s)

MARNETT ET AL.

Examiner

Yong D Pak

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-54 is/are pending in the application.
- 4a) Of the above claim(s) 2,5 and 22-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4 and 6-21 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date see attached.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Claims 1-54 are pending. Claims 2, 5 and 22-54 are withdrawn. Claims 1, 3-4 and 6-21 are under consideration.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1, 3, 4 and 6-21) in the reply filed on June 14, 2004 is acknowledged.

Claims 2, 5 and 22-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 14, 2004.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on January 8, 2002 and February 26, 2002 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Examiner notes that the information disclosure statement (IDS) submitted on January 16, 2002 is a duplicate of the IDS filed on January 8, 2002.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a method of detecting COX-2 activity by detecting metabolites of a substrate that is selective for only COX-2. Therefore, these claims are drawn to a method of using a genus of any substrate metabolized only by COX-2. The genus is highly variant because it includes molecules which differ widely in structure from PGH₂-EA metabolites and includes synthetic molecules which are not derivatives of native substrate of COX-2. The specification only describes arachidonyl ethanolamide as being substrates for only COX-2, leading to the formation of PGH₂-EA metabolites which are then detected. The specification does not provide any partial structure responsible for COX-2 selectivity, or any physical or chemical characteristics/properties of COX-2 selective substrates which endow said substrate with specificity for COX-2 versus COX-1. Therefore, the specification fails to describe a representative species of the genus of substrates that are only metabolized by COX-2.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claim 1.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting COX-2 activity by detecting selective substrates that lead to the formation PGH₂-EA metabolites, does not reasonably provide enablement for a method of detecting COX-2 activity by detecting any substrates that do not lead to the formation of PGH₂-EA metabolites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 1 is drawn to a method of detecting COX-2 activity by detecting any COX-2 selective substrates. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of COX-2 selective substrates and their metabolites encompassed by the claims.

It would require undue experimentation of the skilled artisan to practice the claimed method of detecting any COX-2 selective substrates and trying to detect any of the metabolites formed. The specification fails to teach how to use any COX-2 selective substrates because it fails to give any guidance so that a skilled artisan would be able to identify any metabolites formed by any other substrates as being selective for COX-2 and not for COX-1. The specification is limited to teaching the use of PGH₂-EA as the metabolites for detecting COX-2 activity.

In view of the great breadth of the claim, amount of experimentation required to identify and thereby use COX-2 selective substrates, the lack of guidance, working examples, and unpredictability of the art in predicting which molecules are selective COX-2 substrates, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the method encompassed by the claims.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including method of detecting COX-2 activity using

Art Unit: 1652

any COX-2 selective substrates and detecting the formation of any metabolites. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of which substrates to use and which metabolites to detect is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-3 are indefinite because the phrase "COX-2 selective substrate" is unclear. It is not clear as to how one skilled in the art can readily determine a substrate as being only selective for COX-2.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

Art Unit: 1652

granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Isakson et al.

Claim 1 is drawn to a method of selectively detecting COX-2 activity in a sample by adding a COX-2 selective substrate to the sample and detecting activity of COX-2.

Isakson et al. (WO 97/14679 – form PTO-892) teaches a method of detecting COX-2 activity by detecting a substrate that is selective for COX-2, wherein the COX-2 substrate is added to a sample and COX-2 activity is detected (abstract and pages 3-5). Therefore, the teaching of Isakson et al. anticipates claim 1.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Isakson et al.

Claim 1 is drawn to a method of selectively detecting COX-2 activity in a sample by adding a COX-2 selective substrate to the sample and detecting activity of COX-2.

Isakson et al. (U.S. Patent No. 6,045,773 – form PTO-1449 – reference AW) teaches a method of detecting COX-2 activity by detecting a substrate that is selective for COX-2, wherein the COX-2 substrate is added to a sample and COX-2 activity is detected (abstract and Columns 1-12). Therefore, the teaching of Isakson et al. anticipates claim 1.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Isakson et al.

Claim 1 is drawn to a method of selectively detecting COX-2 activity in a sample by adding a COX-2 selective substrate to the sample and detecting activity of COX-2.

Art Unit: 1652

Isakson et al. (U.S. Patent No. 6,045,773 – form PTO-1449 – reference AW) teaches a method of detecting COX-2 activity by detecting a substrate that is selective for COX-2, wherein the COX-2 substrate is added to a sample and COX-2 activity is detected (abstract and Columns 1-12). Therefore, the teaching of Isakson et al. anticipates claim 1.

Claims 1, 3-4, 6-8, 10-17 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Yu et al.

Claim 1 is drawn to a method of selectively detecting COX-2 activity in a sample by adding a COX-2 selective substrate to the sample and detecting activity of COX-2. Claims 3-4, 6-8, 10-17 and 19-21 are drawn to a method of detecting/measuring activity of COX-2 by detecting PGH₂-EA metabolites, wherein COX-2 activity is detected/measured via standard values/curves, various samples are derived from mammals, PGH₂-EA metabolites are detected via a mass chromatogram or the detection step includes an immunoassay.

Yu et al. (Reference BN: PTO-1449) teaches a method of detecting/measuring COX-2 in a sample derived from a mammalian cell by detecting/measuring a PGH₂-EA metabolites (Figures 2-6 and pages 21182). Arachidonyl ethanolamide (AEA), a precursor for PGH₂-EA metabolites is not a substrate for COX-1 and therefore, the method of Yu et al. only selectively detects COX-2 activity (page 21182, right column, page 21183, right column, page 21184, right column and page 21186, left column). Yu et al. generates a standard value and curve for determining COX-2 activity (Figure 1

Art Unit: 1652

and Table 1). Yu et al. detects/measure COX-2 activity by detecting PGH2-EA metabolites via a mass chromatogram (Figures 3-5) and immunoassays (Figure 2 and Figure 6).

The metabolites detected in the method of Yu et al. encompasses the metabolites recited in claims 7 and 16 because the recited metabolites are naturally produced, enzymatically or nonenzymatically, from upon oxidation of AEA by COX-2. Yu et al. teaches that the metabolites of AA and AEA are identical (page 21185, left column and see KEGG – prostaglandin and leukotriene metabolism – form PTO-892).

Therefore, the teachings of Yu et al. anticipate claims 1, 3-4, 6-8, 10-17 and 19-21.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

Art Unit: 1652

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stichtenoth et al. and Yu et al.

Claims 9 and 18 are drawn to a method of detecting/measuring activity of COX-2 by detecting PGH₂-EA metabolites, wherein the sample is urine.

Stichtenoth et al. (form PTO-892) teaches the use of urine sample for assay of XO activity in general (abstract). From this reference, one of skilled in the art can conclude that urine can be used as a sample for detecting COX activity. Stichtenoth et al. teaches detecting/measuring COX-2 activity by detecting/measuring PGH₂ metabolites in urine samples (abstract).

The reference of Stichtenoth et al. does not teach a method of selectively detecting/measuring COX-2 activity by detecting PGH₂-EA metabolites in urine samples.

The reference of Yu et al. as it applies to claims 1, 3-4, 6-8, 10-17 and 19-21, teaches a method of detecting/measuring COX-2 in a sample by detecting/measuring a PGH₂-EA metabolites (Figures 2-6 and pages 21182).

Art Unit: 1652

Combining the teachings of Stichtenoth et al. and Yu et al., it would have been obvious to one having ordinary skill in the art use urine samples to the method Yu et al. to detect COX-2 activity. One of ordinary skill in the art would have been motivated to selectively detect/measure COX-2 activity in 1 urine sample since the sample can be easily obtained from a subject. One of ordinary skill in the art would have had a reasonable expectation of success since Stichtenoth et al. teaches the use of urine sample for measuring/detecting COX-activity and Yu et al. successfully teaches selective detection/measurement of COX-2 activity in a sample.

Therefore, the above references render claims 9 and 18 prima facie obvious to one of ordinary skill in the art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 10-27, 29-39

and 87-89 of copending Application No. 09/923,637. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are claiming common subject matter, as follows: Claim 1 of the instant application and claims 1-8, 10-27, 29-39 and 87-89 are both directed to a method of selectively detecting COX-2 activity in a sample by adding a COX-2 selective substrate to a sample and detecting metabolites of said substrate. Claim 1 of the instant application detects any COX-2 selective substrate. Claims 1-8, 10-27, 29-39 and 87-89 of 09/923,637 detect metabolites of 2-arachidonylglycerol, which is a COX-2 selective substrate. Therefore, the conflicting claims are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 10/213,633. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are claiming common subject matter, as follows: Claim 1 of the instant application and claims 1-10 are both directed to a method of selectively detecting COX-2 activity in a sample by adding a COX-2 selective substrate to a sample and detecting metabolites of said substrate. Claim 1 of the instant application detects any COX-2 selective substrate. Claims 1-10 of 10/213,633 detect metabolites of amino acid eicosanoid, which is a COX-2 selective substrate. Therefore, the conflicting claims are not patentably distinct from each other.

Art Unit: 1652

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

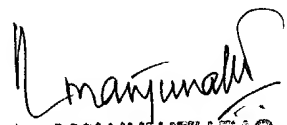
None of the claims are in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner


MANJUNATH RAO
PATENT EXAMINER
Art Unit 1652